Important information. Please read carefully.

VENCID®

PANTOPRAZOLE 40MG
Enteric-Coated Tablet

COMPOSITION
Each tablet contains 40mg Pantoprazole (as Pantoprazole Sodium Sesquihydrate).

PHARMACODYNAMICS
Pantoprazole is a proton pump inhibitor. It suppresses secretion of gastric acid by inhibiting the enzyme system of hydrogen/potassium adenosine triphosphatase (H^+/K^+ ATPase), the 'proton pump' of the gastric parietal cell.

During treatment with antisecretory medicinal products, serum gastrin increases in response to the decreased acid secretion. Also, Chromogranin A (CgA) increases due to decreased gastric acidity. The increased CgA level may interfere with investigations for neuroendocrine tumours.
Available published evidence suggests that proton pump inhibitors should be discontinued between 5 days and 2 weeks prior to CgA measurements. This is to allow CgA levels that might be spuriously elevated following PPI treatment to return to reference range.

PHARMACOKINETICS
Absorption
Pantoprazole is rapidly absorbed with an oral bioavailability of about 77% for enteric-coated tablet formulation, and does not vary after single or multiple doses.

Distribution
Peak plasma concentrations are achieved about 2 to 2.5 hours after an oral dose. Pantoprazole is about 98% bound to plasma proteins.

Metabolism
Pantoprazole is extensively metabolized in the liver, primarily by the cytochrome P450 isoenzyme CYP2C19, to desmethylpantoprazole; small amounts are also metabolized by CYP3A4, CYP2D6, and CYP2C9.

Elimination
Metabolites are excreted mainly (80%) in the urine, with the remainder being excreted in feces via the bile. The terminal elimination half-life is about 1 hour, and is prolonged in hepatic impairment, with 3 to 6 hours for cirrhosis patients.

INDICATIONS
- Moderate and severe cases of inflammation of the oesophagus (gastro-oesophageal reflux disease)
- Duodenal and gastric ulcer
- Eradication of *Helicobacter pylori (H. pylori)* in combination with two appropriate antibiotics in patients with peptic ulcers with the objective of reducing the recurrence of duodenal and gastric ulcers caused by this microorganism.
- Zollinger-Ellison Syndrome and other pathological hypersecretory conditions

DOSAGE AND ADMINISTRATION
To be administered orally. To be used in adults and children above 12 years only.

Once-daily doses should be taken in the morning.

Tablets must not be chewed or crushed and must be swallowed whole with water one hour before breakfast.

Treatment of moderate and severe gastro-oesophageal reflux disease
The usual oral dose is 20 to 40mg once daily for 4 weeks, increased to 8 weeks if necessary.
In individual cases, the dose may be doubled (increased to 2 tablets of 40mg daily) especially when there has been no response to other treatments.
For maintenance therapy, treatment can be continued with 20 to 40mg daily. Alternatively, for recurring symptoms, an on-demand regimen of 20 mg daily may be given.

Treatment of duodenal ulcer
One oral dosage of 40mg daily for 2 weeks is recommended. If not fully healed, continue the same dosage to 4 weeks.
In individual cases, the dose may be doubled (increased to 2 tablets of 40 mg daily) when there has been no response to other treatments.

Treatment of gastric ulcer
One oral dosage of 40mg daily for 4 weeks is recommended. If not fully healed, continue the same dosage to 8 weeks.
In individual cases, the dose may be doubled (increased to 2 tablets of 40mg daily) when there has been no response to other treatments.

Eradication of H. pylori in combination with two appropriate antibiotics
Triple therapy regimen for 1 week.
i) 2 x 40mg Pantoprazole / day
+ 2 x 1g amoxicillin / day
+ 2 x 500mg clarithromycin / day

ii) 2 x 40mg Pantoprazole / day
+ 2 x 400-500mg metronidazole / day
+ 2 x 250-500mg clarithromycin / day

iii) 2 x 40mg Pantoprazole / day
+ 2 x 1g amoxicillin / day
+ 2 x 500mg metronidazole / day

The second tablet should be taken before the evening meal.
The above-mentioned combination therapy usually lasts 1 week and can be extended to a maximum of 2 weeks.
If further treatment with Pantoprazole 40mg is indicated to ensure healing of ulcer completely, the dosage recommendation for gastric and duodenal ulcers must be considered.

Treatment of Zollinger-Ellison Syndrome
An initial oral dose of 80mg daily is recommended, and adjusted as required. Daily doses greater than 80mg should be given in two divided doses.
A temporary increase of the dosage above 160mg of pantoprazole is possible but should not be applied longer than required for adequate acid control.
Treatment duration in Zollinger-Ellison Syndrome and other pathological hypersecretory conditions are not limited and should be adapted according to clinical needs.

CONTRAINDICATIONS
Should not be used:
- in combination treatment for eradication of *H. pylori* in patients with moderate to severe liver or kidney function disturbances.
- in cases of known hypersensitivity to any constituents of the drug or the combination partners.
- with atazanavir.

WARNING AND PRECAUTIONS
Pantoprazole is not indicated for mild gastrointestinal complaints, e.g, nervous stomach.
In the presence of any alarm symptom (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis, anemia or melaena) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment with pantoprazole may alleviate symptoms and delay diagnosis.

Further investigation is to be considered if symptoms persist despite adequate treatment.
In the case of combination therapy, the prescribing information for the respective drugs must be observed.
Patient with severe hepatic impairment should be given 40mg of pantoprazole on alternate day. In patients with severe liver impairment, the liver enzymes should be monitored regularly during therapy, particularly on long-term use. Pantoprazole should be stopped if elevation of liver enzymes occurs.

Pantoprazole, as other proton pump inhibitors, might be expected to increase the counts of bacteria normally present in the upper gastrointestinal tract. Treatment with pantoprazole may lead to slightly increased risk of gastrointestinal infections caused by bacteria (e.g. *Salmonella, Campylobacter* and *Clostridium difficile*)
Regular Surveillance: Patients on proton pump inhibitor treatment (particularly those treated for long term) should be kept under regular surveillance.

Subacute Cutaneous Lupus Erythematosus (SCLE): Proton pump inhibitors are associated with very infrequent cases of subacute cutaneous lupus erythematosus (SCLE). If lesions occur, especially in sun-exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the health care professional should consider stopping Vencid. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Hypomagnesaemia: Severe hypomagnesaemia has been reported in patients treated with PPI like Vencid for at least three months, and in most cases for a year. Serious manifestations of hypomagnesaemia such as fatigue, tetany, delirium, convulsions, dizziness and ventricular arrhythmia can occur but they may begin insidiously and be overlooked. In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPI with digoxin or drugs that may cause hypomagnesaemia (e.g., diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

Fracture: Proton pump inhibitors, especially if used in high doses and over long durations (>1 year), may modestly increase the risk of hip, wrist and spine fracture, predominantly in the elderly or in presence of other recognized risk factors. Observational studies suggest that proton pump inhibitors may increase the overall risk of fracture by 10-40%. Some of this increase may be due to other risk factors. Patients at risk of osteoporosis should receive care according to current clinical guidelines and they should have an adequate intake of vitamin D and calcium.

***Clostridium difficile* Diarrhea**: Published observational studies suggest that PPI therapy may be associated with an increased risk of Clostridium difficile associated diarrhea, especially in hospitalized patients. This diagnosis should be considered for diarrhea that does not improve. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

Vitamin B12 Deficiency: Daily treatment with any acid-suppressing medications over a long period of time (e.g, longer than 3 years) may lead to malabsorption of cyanocobalamin (vitamin B12) caused by hypo- or achlorhydria. Rare reports of cyanocobalamin deficiency occurring with acid-suppressing therapy have been reported in the literature. This diagnosis should be considered if clinical symptoms consistent with cyanocobalamin deficiency are observed.

Interference with laboratory tests: Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. If the patient(s) are due to have a test on Chromogranin A level, Vencid treatment should be stopped for at least 5 days before CgA measurements to avoid this interference (See Section Pharmacodynamics). If CgA and gastrin levels have not returned to reference range after initial measurement, measurements should be repeated 14 days after cessation of proton pump inhibitor treatment.

DRUG INTERACTIONS
- May alter the metabolism of some drugs metabolized by isoenzymes CYP2C19 and CYP3A4 in the cytochrome P450 enzyme system, namely carbamazepine, caffeine, diazepam, diclofenac, digoxin, ethanol, glibenclamide, metoprolol, naproxen, nifedipine, phenytoin, piroxicam, theophylline and an oral contraceptive.
- May prolong the elimination of diazepam, phenytoin and warfarin.
- May reduce the absorption of acid gastric pH-dependent drugs, such as ketoconazole, itraconazole and dasatinib.
- Should not be used with atazanavir as it substantially reduces exposure to atazanavir.

PREGNANCY AND LACTATION
Pregnancy
Pantoprazole should not be used during pregnancy unless potential benefit outweighs risk or clearly necessary.

Lactation
Use of pantoprazole should be made into account the benefit of breast-feeding to the child and the benefit of pantoprazole therapy to the woman

SIDE EFFECTS
Proton pump inhibitors are generally well tolerated, and adverse effects are relatively infrequent.

Common side effects are headache, diarrhoea and skin rashes.
Other side effects include pruritus, dizziness, fatigue, constipation, nausea and vomiting, flatulence, abdominal pain, arthralgia and myalgia, urticaria, and dry mouth.

Isolated cases are such as photosensitivity, bullous eruption, erythema multiforme, Steven-Johnson syndrome, and toxic epidermal necrolysis. Hypersensitivity reactions, including fever, bronchospasm, angioedema, and anaphylaxis can be occurred.

In severely ill patients, effects on CNS include occasional insomnia, somnolence, vertigo, reversible confusional states, agitation, depression, and hallucination are found.

Raised liver enzymes, and isolated cases of hepatitis, jaundice, hepatic failure, and hepatic encephalopathy can be happened.

Rare side effects are such as paraesthesia, blurred vision, alopecia, stomatitis, increased sweating, taste disturbances, peripheral oedema, malaise, hyponatraemia, blood disorders (including agranulocytosis, leucopenia, and thrombocytopenia), gynaecomastia, impotence, and interstitial nephritis.

Subacute Cutaneous Lupus Erythematosus (SCLE)
Skin and subcutaneous tissue disorders
Frequency 'not known': Subacute cutaneous lupus erythematosus

Hypomagnesaemia
Metabolism and nutritional disorders
Frequency 'not known': hypomagnesaemia

Fracture
Musculoskeletal disorders
Frequency 'uncommon' : Fracture of the hip, wrist or spine

Clostridium Difficile Diarrhea
Infections & infestations: Clostridium difficile associated diarrhea

Vitamin B12 Deficiency
Metabolic/ Nutritional: Vitamin B12 deficiency

Interstitial Nephritis
Renal and urinary disorders: Interstitial nephritis

Fundic Gland Polyps (Benign)
Gastrointestinal disorders
Frequency 'common': Fundic gland polyps (benign)

Microscopic Colitis
Gastrointestinal disorders
Frequency 'not known': Microscopic Colitis

SYMPTOMS AND TREATMENT FOR OVERDOSAGE
There are no known symptoms of overdose. In any case, doctor must be consulted.
In the case of overdose with clinical signs of intoxication, the usual rules of intoxication therapy apply.

SHELF-LIFE
The expiry date is indicated on the packaging.

STORAGE CONDITION
Store below 30°C.

PRODUCT DESCRIPTION
Beige, round, normal convex enteric coated tablet.
Available as blister strips of 7's in packing of 14 tablets and 28 tablets per box.
Not all pack size(s) are available.
KEEP OUT OF REACH OF CHILDREN / JAUHI DARI KANAK KANAK

For further information, please consult your pharmacist or physician.

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Manufacturer and Product Registration Holder:
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